Evaluation of a recoil-escape fiber target using $^{94}Mo(p,n)^{94m}Tc$ to produce $^{94}TcO_4^-$ precursor for radiolabeled compounds useful in Positron Emission Tomography.

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Abstract-**A variety of compounds radiolabeled with ^{99m}Tc(140 keV g $T_{1/2}$=6 hours) are widely used in nuclear medicine imaging. These compounds can also be radiolabeled using positron-emitting precursor $^{94m}TcO_4^-$ ($T_{1/2}$=53 minutes) and used with Positron Emission Tomography (PET) to measure tissue concentrations in mCi/cm^3, and produce kinetic data useful to understand the mechanism of drug action.**

This work-in-progress evaluates a novel accelerator target for producing ^{94m}Tc. Positron emitters have been produced with fiber targets, using the principle of recoil escape in which the target atoms are in a solid form, while recovering the product radionuclide ion by stopping it in a liquid or a gas. The recoil ion is transported out of the target, leaving the remaining target material to be used repeatedly in subsequent production runs. Our proposed target is based on this method.

Keywords-94mTc,Positron Emission Tomography, radionuclide production.

I. INTRODUCTION

Technetium-99m dominates the field of diagnostic radiopharmaceuticals by more than one order of magnitude. Technetium-94m permits PET to evaluate quantitatively in-vivo, new pharmaceuticals to be labeled with ^{99m}TC. As with any PET imaging agent the technetium chemist will have the opportunity to measure tissue concentrations in μCi/cm^3 and obtain kinetic data for the compartmental modeling of a new compound to understand the mechanism of drug action. The chemistry and metabolic models of ^{99m}Tc may be used for the positron emitter ^{94m}Tc, in tomographic imaging.

Stone and Christian [7] tested ^{94m}Tc in humans and compared the uptake images obtained with ^{94m}Tc-sestamibi (a perfusion agent) with those obtained using ^{13}N-ammonia. The results of this work support the utility of ^{94m}Tc PET for the *in vivo* assessment of the pharmacokinetics of technetium pharmaceuticals. More recently ^{94m}Tc was used to label antibodies with *anti-carcinogenic-embryonic-antigen* (A-CEA) fragments. These antibodies bind to CEA, a chemical secreted by solid tumors, finding the location of tumors undetected by transmission computed tomography (CT).

Previous experiments demonstrated that the recovery of the recoil isotope was possible only by opening the target, causing high exposure dose to the production chemist.

PET agents have been produced with a slurry target and with a fiber target, both using the principle of recoil escape. The method consists on maintaining the target atoms in a permanent form while recovering the product radionuclide ion by stopping it in a liquid or gas. The product nuclide is transported out of the target, leaving the remaining target atoms to be used again in subsequent production runs.

The $^{94}Mo(p,n)^{94m}Tc$ reaction studied in this project was used previously to obtain ^{94m}Tc, with different target designs.

Previous published works indicate that: enriched (94%) molybdenum-94 has to be used to minimize the production of undesirable isotopes of technetium, and that the most appropriate level of bombardment energies is Ep=13→6 MeV since this range has bigger cross sections with minimum production of the ground state of technetium-94 (^{94g}Tc). Using enriched ^{94}Mo the only unavoidable radionuclidic impurity is ^{94g}Tc, ($T_{1/2}$=4.5 hour). We used three Monte Carlo computer programs, LAYERTAR, FIBTAR, and TRIM, to simulate the reaction and study the experimental phase of the project.

II. MATERIALS AND METHODS

The proposed target is designed with thin molybdenum fibers surrounded by gas (steam or a noble gas). The advantage of steam is that the final product is pertechnetate ($TcO4^-$), which is the labeling agent used in the pharmaceutical kits widely available and used by almost every nuclear medicine department.

Nuclear reaction cross section data are needed for optimizing the production of a radioisotope, especially for calculating production yield and impurities as well as for target design and chemical processing.

Reaction cross-section data are obtained from published work. Ranges of protons in the target

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mixtures and stopping power of the mixtures are calculated using TRIM[13], a program that allows a quick calculation of these parameters for any type of mixture.

Information about the mechanism of a nuclear reaction is often obtained from the distribution of recoil range of its product nuclide. This distribution is frequently required in particle charged particle activation analysis and radionuclide production. These measurements have been done using the catcher foil technique in the methodology and results published by Iwamoto et al[17]. They will be used in this work to analyze the energy of the ^{94m}Tc nuclides recoiling from the molybdenum fibers .

From the conservation of energy and momentum, the maximum and minimum recoil energy can be calculated for a reaction that proceeds via the compound nucleus:

Target Nuclide + Incident Particle
↓
Compound Nucleus
↓
Product Nuclide + Emitted Particle

$$^{94}Mo + p^{+} \rightarrow {}^{94m/g}Tc + n^{o}$$

This concept takes the following mathematical form:

$$E_{pmax}=M_c^{-2}\{[M_e M_i E_i]^{0.5}+[M_e(M_cQ+M_iE_i)]^{0.5}\}^2$$

$$E_{pmin}=M_c^{-2}\{[M_e M_i E_i]^{0.5}-[M_e(M_cQ+M_iE_i)]^{0.5}\}^2$$

E_{pmax} and E_{pmin} are the maximum and minimum recoil energies of the product nucleus (^{94m}Tc) in this case. A negative sign will indicate that the recoil is backward (does not occur in our case).

Following the same criteria the most probable recoil energy is the kinetic energy of ^{94m}Tc and is expressed as

$$<Ep>=M_p\, M_i\, E_i\, M_c^{-2}$$

M_e = 939.56 MeV(mass of the emitted particle)
M_c=174948.37MeV(mass of the compound nucleus)
Mi = 938.27 MeV (mass of the incident particle)
M_p = 87476.31MeV(mass of the product nuclide)
M_t = 87472.06 MeV (mass of the target nuclide)
E_i = 6 to 13 MeV (energy of the incident particle)

Production of ^{94m}Tc recoil energies for 6 to 13 MeV protons are tabulated below

TABLE I
Energy of the recoil ion in function of incident proton energy

E_I	Ep_{min}	<Ep>	Ep_{max}
6	6.46E-05	0.063	0.244
7	7.91E-05	0.073	0.264
8	2.19E-04	0.084	0.283
9	4.14E-04	0.094	0.302
10	6.55E-04	0.105	0.321
11	9.36E-04	0.115	0.339
12	1.25E-03	0.126	0.357
13	1.59E-03	0.136	0.375

It is assumed that the recoil nucleus is formed solely by the decay of the compound nucleus.

These values will be used to calculate the range of ^{94}Tc in Mo. These ranges require the use of fibers with diameters smaller than one micron. Using this data we evaluated the thick target yield and a tentative geometry for the system.

Since the target material is expensive ($6/mg) and not ready available, the system has been simulated using FIBTAR (a computer code based on the Monte Carlo Method that has been written specifically for fiber targets). The code provides the total yield of the system and the recovered yield of the nuclide of interest. It predicted successfully the behavior of previous fiber targets, with experimental results in good agreement with the simulations. FIBTAR is used as a guide to determine the target geometry to be experimentally tested.

III. RESULTS

Extensive simulation of many targets geometries and material mixtures were performed in the energy range Ep=14→6 MeV and Ep=11→6 MeV. These ranges are used in commonly used medium size and compact cyclotrons. Water(liquid and steam), helium, and argon were used as the fluid were the ^{94m}Tc ion will stop and be recovered. Several ratios of gas volume to total target volume (porosity of the target) were investigated.

The recovered yield of ^{94m}Tc is the parameter to be maximized. With a maximum energy of 11Mev the maximum recovered yield obtained is between 9 and 9.6 mCi/μA. When the maximum bombardment energy is 14 MeV, the maximum yield obtained is between 30 and 43 mCi/μA. In a solid target of molybdenum trioxide (MoO_3), we calculated 70 mCi/μA at saturation. This target material requires chemical processing to obtain technetium, and the enriched $^{94}MoO_3$ has

to be recovered (due to its high price) and used again.

Six targets modeled produced high recovered yields of ^{94m}Tc. Three were argon gas and three were steam. Two of these targets are significantly longer, 48 and 22 mm. The other four are 9.2mm long. The inner radius of the chamber seems to be optimum between 6 and 7 mm for all the geometries. The size of the fiber that provides high yields is in the order of 0.04 to 0.2 microns with a separation between fibers of 3 microns, and a porosity of 98%.

The higher yield geometries were evaluated with a heat transfer analysis. The amount of heat in watts that has to be removed is the energy deposited in the target by the beam in MeV times the beam current in μA. Knowing the bombardment energy, the average energy of the protons exiting the target is obtained with FIBTAR, and the heat generated per μA, was used to determine the maximum beam current that will cause no physical or chemical changes in the target. The target material is a porous media in which the thermal conductivity of the metallic fibers is high but the gases are poor heat conductors. The removal of heat required external and internal cooling of the system to avoid the melting of the fibers or the target body.

IV. DISCUSSION

The results obtained with the simulation program are not expected to be accurate. The use of argon as the target gas is an easier approach since is a gas form, however the chemical form of the recovered ion is unknown. Previous targets for the production of different radionuclides added low amounts of oxygen to the inert gas.

Steam has a predictable chemical behavior since the recovered product is likely to be TcO_4^- the recovered product

Once the yield of the nuclide of interest is maximized and the heat generated in the target is removed in an acceptable manner, the next challenge is to obtain molybdenum fibers of the diameters required. Recent developments in nanotechnology regarding microfibers made of molybdenum by electrodeposition offer the best solution[18]. They will have to be fabricated using enriched 94-molybdenum.

V. CONCLUSIONS

Experimental evaluation of the proposed design will require a substantial investment of time and money. Evaluation of steam and argon with added oxygen can be done using natural Mo. The most difficult task will be the fabrication of submicron enriched Mo fibers.

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